>> I’m Jeff White from the Division of Cancer Treatment and Diagnosis at NCI. And together with my co-chair, Gary Ellison from DCCPS, Division of Cancer Control and Population Sciences, that we welcome you to the final session of our four day meeting. It’s been an excellent opportunity to, over these four days, to hear the important research findings and to learn about key issues and a broad spectrum, from epidemiology, cannabis, the impact on, of cannabis on health, in both the positive and negative impact. And to the specific effects of chemical components of cannabis plants and the other synthetic compounds with cannabinoid-like activities. So we’ve - it’s a lot of science to go over. And so what we want to do, recognizing that everyone hasn’t participated in all aspects of the meeting, but to spend some time and allow the co-chairs from the previous sessions to give us a little summary of their session and make some comments about important issues that they think were brought out in each of, I’d say each of the first six sessions. We just heard the last session. And then we will go on to a panel discussion with questions and answers, so you can certainly continue to put the questions in the chat box. But we’d like to use this to do some over-arching kinds of questions would help us understand what’s happening in the science, where it’s going, where it might go, where people think it ought to go and what is necessary for scientific opportunities to be realized. So what we’ll do, as I said, first is to go through from Session I through session VI with the co-chairs and hear their comments and then we’ll get into our panel discussion. So that means we’re starting with Dr. Mia Hashibe from Session I.

>> Hey, and thanks for the chance to do a recap. So our session was on non-medical cannabis use and cancer epidemiology. We covered cancer risk due to cannabis, co-use of cannabis with tobacco and also inhalational exposure from smoked and vaped cannabis. For cancer risk, we reviewed 40 published epidemiologic studies. The results have not been consistent on an association between plant-based smoked cannabis and cancer risk. Since the cannabis use patterns are changing greatly right now with the legalization and the wide range of products, new well-designed studies are needed to investigate cancer risk with the current modes of cannabis use. Including biomarkers covered by Dr. Blunt (ph.) from our session would really enhance the epidemiologic studies. And considering the complexity of cannabis and tobacco co-use, and various modes of use as presented by Dr. Cohen (ph.), will also be important in any new studies. For cannabis and tobacco co-use, we learned that co-users have higher rates of tobacco use. Co-use overlaps with low socioeconomic status, race minority groups, and mental or physical health problems. We learned about blunts, which are created by removing all or part of the tobacco from a cigar and replacing it with cannabis. And blunts are perceived as less harmful and addictive, and this could create a misclassification issue in epidemiologic studies since we do rely on self-reports and sometimes people do not consider blunts a tobacco product. We looked at the trends in the increase in cannabis vaping. And Dr. Cohen also covered that cannabis and big tobacco spending may be contributing to co-use itself. More research is needed on specific subgroups, especially among older individuals who have higher rates of cancer risk, since co-use studies have really focused on younger individuals. And also poly-tobacco use with cannabis use is not studied well. So, poly-use means looking at different types of the tobacco. So that could include cigarettes, cigars, other methods, along with cannabis use. And also in terms of message development, most stakeholders have targeted one single behavior in their messaging. So, it could have been on alcohol only, or tobacco only, or cannabis only. So a focus on multiple substance use behaviors in message strategies is less often taken and some stakeholders may be grappling with how best to address cannabis use in messaging strategies, especially in contrast to tobacco. For inhalational exposure - sorry, there were specific suggestions from Dr. Cohen also to correct misperceptions of co-use harm, to increase funding to understand co-use, and also possibly encourage tobacco cessation in the cannabis dispensaries. In terms of the inhalational exposure from smoked and vaped cannabis, we learned that cannabis and tobacco smoke toxicants are similar in pattern and amount. The exposure to carcinogenic acrylonitrile measurably increases after smoking a single joint. In contrast there was no increase in acrylonitrile after oral or vaped cannabis exposure. And the NHANES exposure biomarker study showed higher rates of PAH and acrylonitrile among cannabis users. In the past study we saw higher smoke exposures in dual users of cannabis and tobacco. In terms of the vaping liquid constituents, we learned that it can be quite harmful when inhaled. And the vitamin E acetate was the primary cause of EVALI, or the e-cigarette vaping associated injury outbreak. So challenges are that we still need data to support the use of cannabis-specific biomarkers in our research studies. Some interesting challenges that were raised in the discussion session were that public health has had a minimal role in regulating cannabis. And the ways that public health could really contribute include data monitoring, as discussed in the previous session, with registries, public education, summarizing how policies are affecting use and also engagement with the public. And there was also a question from the audience about potency and implications on dependence. And since most of the research has been on plant-based smoked cannabis, it’s really difficult to make conclusions on long-term health effects for the current types of cannabis use. And Dr. Shar (ph.) specified that there would be an expected increase in dependence since the current cannabis products are more concentrated and powerful. So our take home message from our session is that we need research in all three areas covered by our session which includes assessing cancer risk, cannabis and tobacco co-use, and also developing cannabis biomarkers. Thank you.

>> Great, thank you so much. All right, and that takes us to Dr. Braun for Session II.

>> What a lovely way to end the conference. So, Session II, entitled ‘Cancer and the Cancer Patient,’ provided introduction to topics covered in greater depth later on in the conference. I’ll briefly summarize its key points and then offer some potential future direction. The session that opened with eloquent testimony from Stacy Blanski (ph.) Cornell graduate and cancer survivor, who detailed the medicinal benefits she derived from cannabis during her cancer treatment. Help with nausea, help with appetite suppression, I mean appetite stimulation, insomnia, and mental health concerns like depression and anxiety. She also recounted the limited clinical weigh-in she received regarding cannabis during her care. Her oncologic team neither discouraged nor encouraged her, and certainly offered no medical advice. She made a bit of a story in the chat function when she confessed that now in the surveillance stage of cancer treatment, she is no longer authorized by her medical team to use medicinal cannabis, despite continuation of target symptoms. Next I spoke. I reviewed the evolution of our current legal landscape, one in which state and federal laws frequently conflict, and the 1970 Controlled Substance Act that continues to render cannabis as Schedule I. In other words, considering it devoid of all medical utility, and more dangerous than cocaine, which is Schedule II. I touched on the conundrum the legal climate creates for medicinal cannabis researchers in the U.S., who contend with a dearth of funding opportunities, avenues to sourced trial drug, and procedural red tape. I also explored the effects of this milieu on oncology clinicians who, evidence suggests, do recommend medicinal cannabis to patients with some frequency, while simultaneously perceiving themselves ill-equipped to make clinical recommendations. And they contend with a dearth of medicinal cannabis clinical guidelines, medical support infrastructure, and CME to support them in their medicinal cannabis oversight. It is no surprise that cancer patients like Stacy Blanski find themselves turning to non-medical and anecdotal information sources. Evan Pergam (ph.), an infectious disease physician at the Fred Hutchinson, gave such a wonderful overview of some of the greatest risks of cannabis use by cancer patients, possible mold, fungal, and other infectious risks. EVALI as Dr. Hashibe just mentioned. He touched on the pharmacodynamics and pharmacokinetic drug botanical interactions. Possible decreased efficacy of some immunotherapy drugs with cannabis use. Not to mention rarer risks like cyclic nausea and vomiting and practical concerns such as dosing imprecision, high cost, the possibility the children could access the product, and legal risks. Donald Abrams, oncologists, integrative medicine doc, cannabis and pain clinical trialist, provided a beautiful far-reaching survey of cannabinoid research supporting symptom targets of greatest interest in oncology. So, conclusive evidence around chemotherapy-induced nausea and vomiting, suggestive evidence for anorexic cachexia, particularly with THC-based medications. And with an amiximal (ph.) and other studies, suggested ancialasis (ph.) - sorry, suggested relief of cancer-related pain. He expressed less confidence that cannabis would prove a robust anti-neoplastic, despite promising signals from pre-clinical realms and called for future investigation in this area. Which brings me to future directions. With the time remaining, I would like to add my two cents to the discussion. When I consider what scientific evidence clinicians hold dearest, it is clinical trials from our agent of interest and our population of interest. So what should be our agent of interest? Well, as this symposium has made abundantly clear, bioactivity comparisons between purified THC and whole plant cannabis are speculative, as cannabis is not one active ingredient, but hundreds that act through complicated synergistic and inhibitory interactions for an ensemble effects or entourage effects. And while some of what is available through the cannabis dispensary is probably pretty purified THC, the bread and butter of cannabis dispensaries are products derived from whole plant cannabis with the hundreds of active ingredients. When I examine oncologic clinical trial evidence collected in, say, the last two decades for these kinds of products, there are few major studies that come to mind. And although research evidence has shown that cancer patients use cannabis through many different routes of administration - combustion, vaporization, vaping, topical applications, to name a few - the oncologic studies that I am thinking of were completed using oral mucosal or oral trial drug administration exclusively. All this to say, when I think of next steps, I think of this: We need additional rigorously conducted clinical trials of whole plant cannabis to assess the benefits and risks of such products for indications that our oncology patients are targeting, the implications cited by both Stacy Blanski and Donald Abrams. We also need comparative efficacy trials between different routes of administration, and concentrations of active ingredients; what the cannabis industry refers to as golden ratios. And we also need dose finding trials. And when we have this data in hand, I have no doubt that the oncologic community will act on it. Members of the oncologic community are some of the most evidence-based clinicians I know. Thank you.

>> Great, thank you so much. So that now leads us to Dr. Lichtman from Session III, Cancer Symptom Treatment Side Effects the Pre-Clinical Session. Dr. Lichtman?

>> Good afternoon everybody. So, just to summarize very briefly this pre-clinical session, the focus was on the endocannabinoid system as well as phyto-cannabinoids, for the treatment of cancer pain as well as the treatment for chemotherapy-induced peripheral neuropathy, as well as chemotherapy-induced nausea and vomiting. And established laboratory animal models have been used amongst many different laboratories which show that both phyto-cannabinoids, as well as targeting the endogenous cannabinoid system, largely through inhibition of the catabolic enzymes of the endocannabinoids and anandamide in 2-AG provide much promise for these kind of palliative treatments. So, to summarize, the work in each group, the presentation by myself focused on 2AG regulating enzymes. And we found that in a mouse model of chemotherapy-induced peripheral neuropathy, studying either the degradade of 2-AG enzyme or the biosynthetic 2-AG enzyme produced a reduction in nociception in the mouse that was accompanied with a reduction of hypersensitivity, of dorsal - I’m sorry, of hypersensitivity of DRG neurons, as well as reduction of inflammation markers in the DRG. Likewise, Sara Ward’s presentation also looking at CIPN, focused on phyto-cannabinoids. And she found that THC as well as a non-psychoactive cannabinoid CBD, reduced the nociception and some of the inflammatory markers in CIPN. And strikingly, Dr. Ward also found that combination of THC and CBD produced augmented or a synergistic anti-nociceptive effects. And again, this kind of plays into that whole idea of the entourage effect. She also looked at a number of synthetic CBD analogs and found enhancement of the reduction in pain in CIPN mouse model. Dr. Piamelli (ph.) gave a broad talk on the treatment of or the targeting of the endocannabinoid system for cancer pain. He reviewed some of the data from clinical trials, as well as gave a very nice overview of the preclinical trials and found that there is promise of cannabinoids in treating cancer pain, but the efficacy is not going to be as strong as opioids. And in fact, there’s some promise that combination of cannabinoids as well as with opioids can lead to some opioid sparing effects and have beneficial effects for the patient. Finally, Dr. Linda Parker reviewed some of her research examining cannabinoids in the treatment of nausea and vomiting, using elegant rodent models of vomiting in a shrew as well as nausea in a rat gaping model. And she found that CBD, as well as CBD acid, with great potency reduced nausea and vomiting behaviors. There was much promise in this, in this preclinical work and there was quite a bit of discussion about its implications in clinical trials. So, I’d like to talk a little bit about future directions. And a major challenge is how to translate this preclinical research into the clinic. And Dr. Piamelli brought up several great points during his presentation and the following discussion. That it’s very important not to look just in one sex, but to look in both males and females and in multiple species. Likewise, it’s important to look at multiple endpoints in terms of nociception, as well as different inflammatory markers. So the more that we could generalize these results across species, the greater likelihood for arguing for a clinical trial here. So there was also some discussion about whether the phyto-cannabinoids are a lower hanging fruit versus the endocannabinoid system. And there are different advantages for pursuing both sorts of targets. So for the future, I think cannabinoids, phyto-cannabinoids, as well as targeting the endocannabinoid system, has promise for the treatment of CIPN as well as cancer pain. But not only that, it can also lead to opioid reducing effects, or opioid sparing effects. So, I think in closing it’s going to be very important for the basic scientists to work closely with clinical scientists to really translate these data in the most productive manner possible. Thank you.

>> Great, thank you. Right, so that takes us now to Session IV, Dr. Mark Wallace is going to talk about the session on cancer symptoms, treatment side effects, the clinical side. Dr. Wallace?

>> Okay, good morning from California. So, our session was focusing mainly on the clinical aspects of the use of medical cannabis. And there were two talks on cannabis and pain relief and the one on well-being. And the reason we chose these is because the most common reason patients are using cannabis clinically are, number one is for pain; and then the following is their depression and anxiety. And then there were a couple of talks on symptom management, including [break in audio], and then anorexia and cachexia. And then the final one was on the role of the clinicians and what we, you know, some of the pitfalls with [break in audio]. The bottom line is that the common theme was that it’s very difficult to translate these preclinical studies into the clinical area. And the main reason is for challenges that I want to bring out. And they’re very common themes across all of them. The first of all, the first challenge is that there’s very a lack of high [break in audio] one’s status of cannabis and making it very challenging to do multi-center trials. And oftentimes most of the data that was presented across all of these presentations were - it’s very difficult, but that the quality of the trials were poor because the numbers were low and randomized controlled trials are very difficult to get funding. And then for those that do get funding, there are regulatory hurdles are enormous, resulting in delays up to two to three years between getting funding and conducting the clinical trials. An example is here in UC San Diego we see funding for a migraine abort trial using cannabis and finally after two years we’re able to start the trial. The second [break in audio]. The federal cannabis is different. The federal cannabis and the extracts are different from real world cannabis. And this is highly variable, especially in the state of California where we’re getting very good at producing very high quality cannabis. It’s probably higher quality than the federal cannabis. An example is the California Bureau of Cannabis Control which is mandated product testing. So, it’s getting very, very high quality, yet we don’t have access to it because of the Schedule I status in the federal regulations. I think we do need more access to what’s being manufactured and what real world patients are receiving and using. We also need to strategize and encourage the FDA to get involved in [break in audio].

>> Dr. Wallace, excuse me for a minute. This is Jeff White. Jennifer, because Dr. Wallace, you’re dropping out at times, we want to see if we can fix this. Jennifer, do you have any suggestions perhaps?

>> Yes, I do. Dr. Wallace, if you could continue maybe without your video that may help.

>> Okay, is this better with the video muted, or at all?

>> Yes, we can hear you.

>> Okay. And so the third challenge were pitfalls for patients when accessing cannabis from dispensaries, even online. It’s just [break in audio]. These are - most of these products that are received online are really ineffective. The ones that are received from dispensaries are way too high in THC content. And they lack of a safety and even appropriate labeling. We don’t even know when the patients bring these products to us and we look at the label it’s hard to determine just what they’re using. And this is also caused by widely varied, wide variations in state laws. So it’s so different between - from state to state. It’s really hard to come up with recommendations. So I think we need to make it easier for compounding pharmacies to compound these cannabinoids, and take the medical use out of the hands of the dispensaries. Again, Schedule I status is a big barrier for this. There’s also the issue of recreational use being very different from medicinal use and the recreational laws are starting to kind of infiltrate into medical use. And we need to educate our patients on the difference between medical use and recreational use. And educate [break in audio], the effects of these THC and CBD are very, very different from higher doses. And they have actually often - oftentimes they have opposite effects and even a very negative effects with higher doses of THC. There is a huge need for providing training for the clinical use of medical cannabis. And [break in audio] brought out in the final - the clinician’s role in medical cannabis care. Most healthcare providers just have no idea how to and how to recommend the medical use of cannabis. And then finally, the last challenge is that we need to integrate the medical use of cannabis into the patient’s healthcare and medical records. So thank you, that’s our summary.

>> Great, thank you, Dr. Wallace. I see that we accidentally left off Dr. McAllister from Session V, the Cancer Biology Prevention session. I’m sorry, Dr. McAllister for that omission, but we certainly do want to hear your comments. I think you’re muted though. You need to unmute.

>> There we go. Thank you. Good morning from California. Yes. So, our session started out with Dr. Mary Abood (ph.) reviewing cannabinoid signal transduction. She talked about cannabinoid receptors, the endocannabinoid system, and control of physiological functions in the body by these systems. And then also talked a little bit about some of the neuro research with the additional receptors that have been defined as cannabinoid-like. Dr. Manuel Guzman (ph.) then did a review of preclinical data in cannabinoids CB1 and CB2 receptor agonists, particularly THC. Controlling many aspects of cancer progression in preclinical models, such as proliferation, invasion, metastasis, angiogenesis. And of course had a bit of a focus on atopic mediated cell death. I talked then about cannabidiol mediated anti-tumor activity in preclinical models. Again, CBD doesn’t act in it efficiently with CB1 and CB2 receptors. So a different mechanism of action is implied in comparison to CB1 and CB2 receptor agonists such as THC. I reviewed the data in this space which in comparison to CBD there is very similar activity across cancer progression in preclinical models. Again, inhibition of proliferation, invasion, metastasis. I focused a bit on targeting of a gene called Id1, and then reviewed all the other major pathways that have been implicated in the anti-tumor activity of cannabidiol. A very interesting, intriguing talk by Dr. Joe Califano (ph.) showing that cannabinoids actually can stimulate HPV-mediated oral pharynx cancer. So, but it was very specific for this type of cancer. And he talked about the implications of the stimulation of the stimulation of MAP kinase in this cancer for the stimulation observed. But very intriguing work. And really the take-home message is that there may be specific cancers that really aren’t indicated for treatments. We all agreed that, and I think this has been a theme throughout these talks, that what’s really an important next step is moving towards well-controlled clinical trials. But in addition to that, we really also, on the basic science level, need much more preclinical work, particularly in understanding the neural cannabinol control in general of cancer progression. My interest again is trying to find these initial interaction sites for CBD that results in these downstream effects that lead to an envision of cancer progression. And again, much more preclinical work to look at. So, in terms of next steps. Some points of interest are really, again, unraveling the role of endocannabinoid system in tumor biology, and also what aspects of the tumor micro environment are most important to the cannabinoid control of the cancer progression. Really is there any evidence actually for cannabinoids that are influencing epigenetic processes and the consequent gene expression. Something that came up also a few times is really defining biomarkers that predict response to cannabinoid anti-tumor action and Dr. Manuel Guzman group had done some of these work. And so they talked about in the space of the resistant glioblast stem or brain cancer. And so, to end, we really want to go in greater depth to look into the basic biology of the ability of cannabinoids not only to inhibit cancer progression, but also it appears in certain cases, certain types of cancers, they may stimulate. So this would be really important to understand the differences in this fundamental biology behind these outcomes. So thank you.

>> Great, and thank you. And so then we’ll next hear from Donald Abrams who was the co-chair with me of the Session VI on cancer treatment preclinical and clinical. Donald?

>> Thank you Jeff, and thank you again for hosting this very wonderful get-together. Really fabulous. Our session had two preclinical presentations and two rather complementary clinical presentations. We heard from Guillermo Velasco who works with Manuel Guzman, who essentially expanded on what Sean just mentioned Manuel said, talking about glioblastoma as a good candidate for assessing the effects of predominantly THC on the decreased proliferation, decreased angiogenesis and invasiveness, and increasing apoptosis via autophagy. He also brought up some work that they’re doing now on looking for resistance to cannabinoid anti-cancer activity by using gene analyses. And what I found really interesting was that the ALF mutation seems to lead to resistance to the cannabinoid therapies. And if you inhibit ALK, that re-sensitizes the tumors to THC. He also expanded on the work that THC in the glioblastoma preclinical models seems to enhance the activity of Temozolomide which is the main chemotherapeutic agent that we use. He did end by suggesting that THC needs to be in the mix when we’re looking for anti-cancer activity of cannabis and cannabinoids. We then heard from Ramesh Ganju from Ohio State who was more interested, as Sean McAllister, in CBD and its anti-cancer potential. And he focused originally on the CB2 receptor, which he says is highly expressed in the immune system cells and CB2 expression correlates with prolonged relapse-free survival in patients with triple-negative breast cancer. So he talked about CB2 agonists that inhibits triple-negative breast cancer growth and metastases and noted that in CB2 knockout mice, that allows for enhanced tumor growth. So his suggestion is that CB2 activation enhances the recruitment of CD8 T-cells which are cancer cytotoxic cells. And he feels that CBD enhances drug uptake and apoptosis as well, and inhibits migration, similar to the work from the Guzman-Velasco team on what THC does. But it was, as opposed to direct cytotoxic effects, it was more of an immune-enhancing effect of CBD via the CB2 receptor. We then moved on to the two clinical trials, or clinical investigations. The first from Professor Twelves from Leeds in the United Kingdom. A long-awaited, deeper dive into their randomized placebo-controlled trial of nabiximols, the oral mucosal spray with the one-to-one ratio of THC to CBD in patients with recurrent glioblastoma. Where they were treated, twelve patients after the short six patient phase I study, twelve patients were randomized to add nabiximols to their chemotherapy, and nine added placebo. And these results which were initially presented in February of 2017 are now awaiting publication in *The British Journal of Cancer* again, perhaps demonstrating that there is some delaying in getting results of these clinical trials published in the medical literature. But the results clearly demonstrated an advantage with regards to not necessarily progression, which appeared to be the same, but overall survival was quite different. In that at 12 months 83 percent of the nabiximol group compared to 44 percent of the placebo group were alive. And they estimate the overall survival as 21.8 months for the nabiximol recipients and only 12 months for those who added placebo to their standard treatment. So this is the first randomized placebo-controlled trial, albeit very small, suggesting that there is some potential benefit to adding at least a one-to-one THC to CBD substance to standard conventional cancer therapy. And again, doctor - Professor Twelves was very aware of the fact that it is a small study and it was not, in fact powered, for survival. The last study that we heard was a prospective analysis of Israeli patients from Gil Bar-Sela at the Emek Medical Center in Israel. His group had previously published a retrospective review suggesting that in patients receiving nivolumab, the PD immunotherapy, had less tumor responses for lung cancer, kidney cancer, and melanoma, compared to patients who were just getting the nivolumab alone. That is, cannabis in association with the immunotherapy seemed to decrease progression, but had no impact on survival. More recently they did just publish an article this year in *Cancers* which shows in the prospective analysis that cannabis consumption did in fact impair survival in patients who used it in association with immunotherapy. Interestingly, the patients in the group that was using cannabis with immunotherapy were more likely to be getting their immunotherapy as second or third line. A much statistically significantly larger percentage of patients not using cannabis were getting first line immunotherapy, and I sort of quizzed him on whether or not that might be accounting for the difference that they see. In addition, there’s no information in this manuscript or in his presentation on the PDL1 status of the tumors from those patients, which probably is the single most important prognostic implicator. He did note that the patients receiving or using cannabis in addition to their immunotherapy had less immune-mediated adverse effects. And recently a paper was published suggesting that people who get the more immune mediated effects from their immunotherapy are those who have better outcomes. So they postulate that cannabis has some anti-inflammatory or perhaps some immune-suppressant effects that may be impacting with the effect of the immunotherapy. But I think again this is not a randomized placebo-controlled trial and there seem to be many other confounders and some absent information that might be beneficial. However, as I mentioned during the question and answer period, this is important because for me this has been somewhat of a practice changing or patient informing result. I do try to tell all patients who are receiving immunotherapy and may be contemplating or using cannabis about the results of this, the retrospective and now the prospective non-randomized trial. So, future directions, obviously we need more information on whether or not cannabis is in fact interfering with immunotherapy, as immunotherapy is becoming, in fact, first line treatment for many different cancers that we see. We need more clinical trials, but it was reported that pharmaceutical companies are not really interested in developing cannabis botanical trials, and more interested in looking at isolated cannabinoids and terpenoids. And then it was recommended that perhaps we should gather data from natural experiments that are happening everywhere all the time, i.e., rely more on observational studies. But again, even the prospective is really observational study as I point out does have potential for confounders which makes interpretation difficult. So I think we all agree that this question of whether or not in humans cannabis has any anti-cancer activity is one that is yet unanswered and certainly warrants further investigation.

>> Great, great - thank you so much, Donald. So I’d like now, since we’ve just heard the Session VII, I asked Dr. Cooper just to join us in the panel as opposed to give us a synopsis of that. So I’d like if all of the co-chairs could turn on your videos and we can start into a Q and A session. And I’d like to turn it over to my co-chair to start that off.

>> Good afternoon, everyone, and thank you for a wonderful panel summary. I appreciate all you’ve done, and I’d like to also thank all the speakers who were involved in this conference. This has been a week full of information. I can’t tell you how much I’ve learned over the last four days and I appreciate each and every one of you. We’ve heard a lot about the current limitations in terms of the DE Case Schedule One for doing research. I want to preface my question with some of it being said we’ve been doing it in CI. We talk about real-world data. One of the things that we’re doing is we’re conducting a survey of cancer patients across the United States, collecting information on their cannabis use, including current and past use, frequency and duration. Also, the therapeutic reasons for use. We’ll have information on tumor type and it’ll be among, about 12,000 patients. The other thing that we support are cancer epidemiology cohorts. Some of these cohorts are aging. They’re long-term follow-up cohorts and some of them are collecting information on cannabis use in the general population. And then we have a funding opportunity announcement available now for new epidemiology cohorts focused on the environment and cancer, and that could be an opportunity for further research on this topic. So given what I’ve just presented, a question is regarding how epidemiologic or observational studies of real world cannabis use can play a role in fielding evidence surrounding this topic. And what kinds of questions should we be asking, are we too limited because we can’t tease out the chemical constituent, potency of the products being used? So I’d like to open it up for the panel to address that. Thank you.

>> So I think there’s multiple (unint.) to this. A new cohort study would be really great, since you could capture a lot more detailed information on the current modes of use. And the challenges that a new cohort, it takes time for the results to come in, since it takes decades for the cancer to develop after the exposure. Another approach would be the cohort consortium analysis. And Dr. (unint.) was kind of enough to email an update about the consortia. So he actually surveyed, back in 2014 which cohorts had collected information on cannabis and 55 cohorts were surveyed and 51 responded. And there are a handful of cohorts including the sister study that has cannabis information. Of the cohorts that I presented in my review, some of them were based in Kaiser in northern and southern California. So those are possible, the data is there now that we could possibly look into. And then the third approach that is possible is that some of the cohorts might be willing to add new questions on cannabis as follow-up questionnaires. So there were two cohorts that indicated that they were willing to do that. And also I was starting to look in the questionnaires a little bit and the California, I think it was the teacher study recently added cannabis into their 2015 - or ’17 to ’19 follow-up questionnaire. So that’s a possible approach that’s a little bit more hybrid in utilizing cohorts that are existing and not having to start a new study. But - oh, sorry.

>> Yeah, I just wanted to follow up with that. Because Dr. Abrams mentioned, you know, one of the issues with follow up studies being, you know, the inability to control for confounders. And so what kind of questions should we be asking in addition to the information that we collect on cannabis use? What are the potential confounders that we should be considering?

>> Right. So, I mean, tobacco clearly would be the biggest confounder we’re worried about. We’re also worried about alcohol use for the cancer risk. But those can be collected in detail. And I think pairing that with biomarker studies would really enhance that as well. So the - Dr. Blunt’s presentation covered the different components that can be captured. So that would be a really powerful study, if you can combine both self-report and biomarkers, whether it’s urine or other bio samples.

>> Thank you. Anyone else want to comment?

>> This is Mark Wallace. These epidemiological studies, one of the risks and the challenges is that if you don’t know what these subjects are using, you can get very wrong results and invalid. An example is, in the study done in Australia [break in audio] cannabis to treat pain. And they concluded that the cannabis increased pain, it increased opioid use, and it worsened outcomes. The problem with a study like that is that they just combined everybody and that you didn’t know if the subjects were using it recreationally or if they were actually using it to treat their pain. And so [break in audio] using, you can get invalid results. So, and this is where the challenge [break in audio]. You’re probably - it would probably help to work with the manufacturers that are developing it and distributing it so we know what they’re getting.

>> Yeah, well, so I agree with you on that. And we would need to tease those effects out. But I think I heard you say that even with the dispensaries, the products that the folks are using, we don’t have a really good idea of what they’re using in terms of the THC content, the CBD content. So even using those data would give us potentially wrong answers. Is that right?

>> The answer is yes and no. And the challenge is, is that the state laws are so variable. So you have highly variable quality control from state to state. So even in California - now, California has gotten pretty good because they started the Bureau of Cannabis Control, which was put into law in 2018. They are failing a significant number of products, meaning they’re failing them so they cannot go to the dispensary shelfs. And then you have other states that don’t have those kind of laws. And so you don’t know what [break in audio]. So the answer is yes, even at the dispensaries. But that will vary from state to state.

>> Thank you. And before we move on, does anyone else want to comment on the utility of epidemiologic and observational studies and the kinds of questions we need to be asking?

>> Yeah. So I agree with Dr. Wallace that this is an imperfect science, but I do support still these kinds of pragmatic types of studies. I think it’s really important to do a deep dive, nonetheless, into what patients are using. And I think it’s important to do a deep dive into who they are, because I don't even think we know that. I don't think we really know, is it cancer patients in active cancer treatment who are using cannabis, or is it cancer survivors, like Stacey Blanski, who hopes to still be using it for residual symptomology. Like we don't even know, and we shouldn’t make assumptions. I think we need to know as best we can what do they think they’re using with the content. I think we need to know the chronicity of their use, like are they using it, I don't know, once in a blue moon or are they using it as an as-needed medication? Are they using it as a standing medicinal? Why are they using? Are they using for the same reason that their certifying physician thinks they are using, or are they using it for a different reason? How are they using? So few of us ask, like are you smoking it, are you vaping it? Like how are you using it? And I think we’ll be surprised by the answers. I think we’ll find that patients use it many different types of ways, depending not their mood or other indicators. Who is advising you around your use, and who isn’t advising you around your use that you wish would? And then, of course, the risks, the perceived risks, I think those are important too.

>> Thank you. Dr. Braun.

>> I would just like to add that I mentioned, I think yesterday, the Israeli study of 2,000 cancer patients who got licenses to use cannabis in Israel. And they get interviewed at baseline and then at six months. And what’s reported in the manuscript is that their pain decreased significantly and all of their other symptoms decreased significantly by six months. But the issue is, maybe that’s because their cancer was cured and they didn’t have nausea anymore or pain or insomnia in that six month period. And that’s just one of the problems of collecting observational studies without getting all the information that you need.

>> Jeff? Go ahead.

>> Okay, I’ll chime in here and say that you know, all the respondents to this question have demonstrated the need for certain questions to be asked regularly. And I think that this demonstrates we need a uniform set of questions that we can put into our studies where at some point in time all the data can be put together. So how people are using it, how many milligrams of THC, if possible, CBD. What the intention of use is, so that at some point in time we can compare our results at one university or one site to another site. I think that’s really important moving forward. And there has been some movement. So NIDA has put out questions that are being used about cannabis use and why it’s being used and mode of use. Of course, part of the issue is that the popular modes of use right now might be changing in the next two or three years, as we’re seeing. So the industry is rapidly evolving. But if there’s some way - and I’m not an epidemiologist, but if there’s some way for researchers to get onboard and be able to ask the same questions in a systematic way, I think that would really help to drive this research forward. And I do think it’s important in providing not just, you know, what’s happening out in the public, what are people using, what are some of the adverse effects, but these data are important in informing clinical trials going. So it gives the signal to people that are interested in doing clinical trials what doses of CBD are people reporting are effective, how long do people have to be using it for? What mode of use? I do think that it really provides important information for other types of studies down the line.

>> Thank you, Dr. Cooper. I want to put a pin on that and just say that with the cancer supplement that I mentioned, we’re collecting data from cancer patients, there are a core set of variables regarding cancer use that we’re asking them to put in their surveys. And we’re asking all twelve centers that we fund to standardize those across projects. So I think that’s a start to what we need. Jeff?

>> Just a little on the CBD side of things. Because we heard a lot about CBD and my opinion is that the doses that are being used are therapeutic doses. And the reason is, it’s cost prohibitive. If patients were to get the doses of CBD that would be therapeutic, it would be in the thousands - impossible. So we need more studies on those therapeutic - what should be therapeutic doses in the hundreds of milligrams of CBD. That is not happening right now in the, kind of the real world CBD market. It’s much, much lower than that.

>> So maybe I can ask then a question that has come up from some of the speakers about the availability of industrial partners for re-agents for drugs and development and the extent to which that may be limiting the progress of research in this area. Does anyone want to - I mean, our perspective, I think, of the panel that we have here, we are all talking about the U.S. So in the U.S. availability, does anyone want to comment about industrial partners both for clinical re-agents and for clinical re-agents? Talking obviously about therapeutics now.

>> We really don't have a major, a major company in the United States that can provide at least synthetic cannabinoids, that I’m aware of. There used to be one company called INCES (ph.) Therapeutics, but they went bankrupt. And so really, I’m not aware of any companies that you are able to do that. Mostly, it is all surrounded around dispensaries supplying compounds. But correct me if I’m wrong, if someone knows another company out there.

>> Sean, I think GW Pharma is available to supply.

>> I was specifically talking about the United States. Again, GW, as you are probably aware, it’s very significant progress. I mean, a lot of work to get your DEA license, do all the oversees. I’ve done this before, so I know. It’s very - you know, it’s not convenient and it tends to drive researchers away from this space. I think one question that actually, and perhaps this can be answered, I might have missed it, so now that CBD from hemp, verified CBD from hemp is not considered scheduled, will NIDIS CBD or CBD contained from vendors such as Sigma not be considered schedule as well? I couldn’t get that answer. And I say that because I’ve had many like young researchers come to me and say - I’d love to do this research and I’m excited to do it. And then I tell them they need a DEA license, it’ll take them a year to do the research, and it scares them away. And so it’s a real problem, getting young minds interested in the space. Does anyone have any information on that?

>> So I’ll chime in here, if it’s okay. Sean, you raise an interesting point about investigators who want to come in and they get daunted by the process. And this whole CBD issue where yes CBD that is synthetic is still considered Schedule I, which is complicated. So INCES, although it’s bankrupt, it was bought by another company and their synthetic CBD is still around, and in theory could be used for research. But it’s Schedule I. There are other companies with proper licenses that do make cannabinoids that meet FDA standards that can be used for research. And then with respect to hemp-derived cannabinoids, there are companies that are coming up that are making products that would meet FDA standards. So, it’s hard to find that the companies that will work with you and that have the proper documentation of how their products are being manufactured, and have the licensing, they do exist. And I will say from personal experience actually, NIDA has helped a tremendous amount for me, connecting me with companies that have been able to help. So, they’ve been enormously helpful. And also talking to other researchers in the field, I feel like there’s a growing network of us who have managed to make headway in this field. And keeping in touch with those researchers helps other people streamline the process and overcome these obstacles that can sometimes just seem totally impossible.

>> Yeah, no, I thank you’re very much Dr. Cooper. I definitely, I mentor - I have mentored a few people in getting their DEA license to use cannabinoids. I guess my comment would be we want to move away from having CB scheduled so that we can get young scientists involved in this field. Because it’s - that’s too much of a - it really is a bit too much of a burden to ask somebody to wait one year to start their research. So I think really maybe what we need to do is find a hemp supplier that makes CBD up to our standard, and then we can just bring that into the lab. I mean, would that be a workaround? I’m just brainstorming here a bit.

>> For what it’s worth in the clinical realm, I am running a clinical trial at the Zena Farburg in which I am prescribing the GW CBD product to patients off-label, and that seems to get around a lot of the issues.

>> Okay. That’s good to know.

>> So, I just want to say that I’ve been asked by a friend and colleague on the East coast as I mentioned, to be a reviewer of grants. He has a cannabis grower who’s going to donate cannabis and a significant amount of money to do research. And this was one of the questions that I brought up on our last panel, is this okay? And I thought in a discussion with Nida a few years ago about this. That if the product met good manufacturing procedures, that they would say it’s okay, and then it’s up to the FDA. So it’s sort of a catch-22, you know, Escher hands drawing hands thing. But this person seems to be moving forward with accepting this cannabis and money. Whether or not that’s legal, you know, remains to be seen.

>> So I have a comment on the issue of the synthetic cannabinoids. And one thing I do tell [break in audio] that it is, it’s going - it would be a challenge to develop a synthetic cannabinoid, and when it reaches the market it is going to [break in audio] with the natural product because it is so widely available. And that’s another challenge that you’re going to be faced. You maybe, get this approved and then it’s going to be very, very difficult to market - market it. Because our society looks at the natural product as a more healthier product as compared to a synthetic.

>> That’s a great point. From some of the research that we did here, it does sound like, I’m glad you’re bringing this up, that synthetic cannabinoids have some unique properties that not only may be concentrations, but actual the ways in which the biological pathways that they work through. And granted, this - all this - that doesn’t take it away from the competition against natural products, but they did seem to have some unique properties. And what I want to hear a little bit more about is, for these synthetics, are there aspects of those compounds that you think are so unique compared to the phyto-cannabinoids that will push them ahead in clinical development, although they may have some also unique toxicities that would be concerning?

>> One thing that may make them advantageous is the methods to improve the absorption. Because the absorption of the natural extracts are very erratic, very delayed. One thing with the INCES product, was that it’s a synthetic that has a much better absorption profile than Dronabinol which would be its competitor. Now, another thing that you have to be careful with these synthetics is that you don’t want to overstimulate a cannabinoid system because if you do, you’re going to have really negative effects. And that’s where some of these synthetics may be too strong. And we know that these natural - like THC is actually a very weak agonist and a very - it doesn’t have a very high affinity for the receptor. Which actually is probably a good thing, because you don’t want to overstimulate the cannabinoid system.

>> So when we’re talking about the endocannabinoid system, I think we can’t leave out the inhibitors of the primary derivated enzymes for anandamide and 2AG. The FAAH F-A-A-H and mono-glycerol lipase. And you know, the FAAH inhibitor has been brought into clinical trials by Pfizer. It’s available. There are ongoing clinical trials. And the same thing with MAG lipase inhibitors. So these are other avenues to pursue and they lack a lot of the same side effects that you see at least with CB1 agonists like THC.

>> I will say also that as a pharmacist interested in individual cannabinoids and individual terpenes, it is helpful to have synthetic products available because I am interested in knowing specifically what that cannabinoid does by itself and then in combination maybe with some other cannabinoids. And I could only really do that study under very controlled circumstances where I have that cannabinoid isolated. So whether it’s isolated from the plant or it’s synthetically made, in either case, you know, for my work that’s really important to have the isolated component where I can add to that isolated component other cannabinoids of interest or other terpenes of interest.

>> So, thanks, this is a very engaging discussion. We’ve talked about the deeds with regard to epidemiologic and clinical studies. I want to get a little bit into the weeds. There’s a comment in the chat box that suggests that dose of cannabis alone is not enough and we need to be considering individual susceptibility, genetic polymorphisms that may regulate metabolism in this. Does anyone want to comment on that? Are there any studies addressing that at all?

>> Looks like you’ve stumped the panel there.

>> Yeah. There’s not a lot of good studies, sorry.

>> There is this question.

>> Well I guess we need to put that on the list.

>> That’s right.

>> Kind of building on that, it kind of came to my mind that if you think of an individual’s susceptibility of using cannabis for medical use, we haven’t talked at all about some people in the population are already at higher risk due to genetic factors like (unint.) C-1-2, or Lynch Syndrome. And are those populations okay to use cannabis as a cancer patient in case they have a higher risk of a second or a third primary cancer? I think that would be important to consider as well.

>> It’s a great question.

>> Yeah, I think maybe staying in the general ballpark of what we were talking about is, when I asked about biomarkers it goes to what I think Gary was asking. Are there - what kind of work is needed to better identify biomarkers of exposure, or then the other side is biomarkers of clinical efficacy, although that’s very broad. Like not necessarily tumor response biomarkers, but I’m thinking - well let me not qualify it. Let me just leave it at that - biomarkers of exposure and then biomarkers of efficacy. Is there work going on now that needs to be amplified or what do you think needs to be done in those areas?

>> Well that one I can address. That there is really, at least in the preclinical work, looking at cannabinoids as anti-tumor agents or potentially endocannabinoid inhibitors. I’m not aware of any good PK PD studies that have been done in preclinical models and that’s an important piece of information. I mean, most drug companies when developing a drug, an anti-tumor agent, they’ll have that type of data upfront before they really move to multiple models. And I think the problem with those studies is they’re not very exciting. They’re not easy to publish on. And they’re definitely - if you’re trying to put those in your grant, you can - that can - but they haven’t been done and I think they’re quite important. I don’t think we know anything about PK PD profile in the preclinical models. People generally pick a dose that’s been shown by other people in a study to work and they work with that dose. And that’s about where it goes.

>> If I could speak on the pain side of things and biomarkers. And we’ve been searching for biomarkers for pain outcomes for decades and it just hasn’t come to fruition. We’ve looked at functional MRI scanning as a biomarker. We’ve looked at blood cytokines. And we’ve been looking at quantitative century testing. And it’s just never really - we haven’t found anything that’s really predictable and consistent. So there is a biomarker in the - it’s called the - through the Heel Initiative. And the Epic Net. Which there is a biomarker group in that consortium that is trying to give recommendations to NIH on biomarkers. But the bottom line for pain, we just don’t have a biomarker at this point.

>> And let’s just talk about primary endpoints for pain, Mark. You know, the numeric reading scale, the 0 to 10, how much does this hurt? It is so prone, you know, to expectation and placebo effects and it really doesn’t capture what’s going on in the patient’s life, you know, in terms of quality of life. So I think there are a lot of other instruments that we should really champion instead of this relatively crude assay, “on a scale of, you know, zero to ten how much does it hurt?” Well you know looking at quality of life issues, sleep issues, are you eating, are you working, that is a much better endpoint for looking at pain at least.

>> So I completely agree. And there was an NIH-sponsored endpoints conference and that was the common agreement that the linear ten point scale is not [break in audio], but it’s really probably the best thing we have so far. There was a lot of talk on coming up with composite scores, [break in audio] versus and the pain relief and sleep and function and mood. But the challenge with that is that there it’s variable between pain syndromes of which one is the most important. And so if you want to use composite scores, you probably would have to come with a weighted score that would vary from pain syndrome to pain syndrome. It’s just so challenging. Pain is very, very difficult too, and challenging to study.

>> So, we’ve discussed over the last four days wide ranging issues with regard to research in a number of different outcomes using different methods and models. And as we were thinking about, you know, the next steps and how we can accelerate the pace of science, even understanding that we have these limitations with DEA Schedule I. Can someone speak to how you might envision the different disciplines working together to and informing each other in accelerating the pace of scientific discovery regarding cannabis and cancer?

>> So, Gary, great question. And you know, one problem is we work in our little siloes often. So as preclinical pharmacologist, you know, we’re very good at treating pain in our mice and rats, but there are often major challenges in generalizing those results to, you know, to a human condition. So, I think working more closely with clinical scientists and basic scientists together we could come to terms a lot quicker. You know, what are the best targets, what are the best tools to move forward? I think that would help a lot, you know, whether we’re looking at phyto-cannabinoids or synthetics or the endocannabinoid system.

>> Thank you. Anyone else want to comment on that?

>> Our session was quite multidisciplinary, and I think epidemiologists along with different laboratory scientists developing biomarkers and then people specifically studying co-use. I thought I understood the different types of use. I especially worked for tobacco alcohol assessments from people, but I learned a lot from Dr. Cohen. So, I think across those three disciplines we could create a really amazing study.

>> So I’m going to ask a question about the translation from the preclinical setting to the clinical setting and I think this is always a challenge. And in maybe cannabinoids, I don’t know that it’s any necessarily harder, as we just talked about with purified molecules as opposed to the extracts. But sometimes consortia are developed to try to improve translations like that. And I wonder if people think that multi-center consortia or something that will be - that they’ve either experienced some examples of that, or if they have thoughts about the, you know, the potential value of that or versus the centers of excellence within a single institution. I mean, these are kind of the specific mechanisms I'm asking about. But let me just ask from the experience point of view, have you experienced those kinds of environments and you think on the basis of those experiences that you’ve seen value one way or another? I know this is kind of a small community of researchers. Maybe that’s affecting it.

>> Yeah. Donald here. And I think that as a member of a practice based research network in integrative medicine, I think that it does allow, if you have a consortium of sites that are across the country, it does allow for increased enrollment into clinical trials, as I mentioned. And as Chris Twelves demonstrated, that it is sometimes difficult to enroll patients into these cancer cannabis studies. So I think having it multi-centered would be an interesting idea. The problem that I foresee is that it just multiplies the complications of the regulatory approvals if you’re dealing with many places in many different states that have many different attitudes about cannabis and their - the presence of it or absence of it in their state formularies. So I think better than a center of excellence, having a consortium might be an interesting approach, if it doesn’t cost too much to fund the infrastructure for such an endeavor.

>> Well, Don, if you [break in audio] you failed cannabis cancer trials remember through the CNCR because we couldn’t enroll any subjects and we, after two years, we had to stop the trial. One thing that it’s very, very challenging to enroll cancer patients into symptom management trials. And maybe you need to think of it differently as we worry about studying these in the actual cancer pain population, if it comes like for instance do pain therapeutic trials and non- cancer pain. But I really think they can be applied to the cancer pain population. But I agree, consortiums are the way to go and we all need to wait and see how successful the Epic Net is, which is an NIH funded initiative which is a consortium. With a - the data center and then the main center and then you have these specialized clinical centers, of which there’s 14 of them. And the goal is to [break in audio] the clinical trial process. And we’re doing it for at the phase II level. So it’s definitely a way to go, develop consortiums to increase the clinical trial enrollment.

>> Thank you. So I got a signal that we need to wrap up, but I wonder if there’s a way, if I could ask the question about if there are ongoing or planned studies that any of you are aware of that you think others ought to - or that you’re particularly interested in seeing the results of, or things that you - so, yes, ongoing or planned studies, anything that anyone wants to throw out as something that needs to be watched?

>> So I just want to comment, and it doesn’t - it’s not that this necessarily sort of applies to it, to cancer pain, but we are starting the first cannabis study in migraine abort which is, the cannabis products are actually coming from NIH. And it’s going to be a four-way crossover trial, placebo-controlled, with pure THC, pure CBD, THC’s CBD combo, and placebo. And then they’ll be given four bottles and when they have their migraine they will be given the bottle A, and it’s going to be vaporized inhaled cannabis. And then they go to their next migraine. And so that’s going to be about an 80 to 90 subject study, which we just started enrollment.

>> Bob, I’d like to also chime in on some really nice translational work that’s being done at Columbia with Meg Haney and Deanna Martinez, where they’re taking their awards findings that she presented a couple of days ago, looking at how cannabidiol can reduce neuropathic pain induced by chemotherapy. And they’ll be investigating this, or they are - they’re currently doing it right now. They’re looking at cannabidiol for chemotherapy induced neuropathic pain. So I think it’ll be really exciting to see what happens with that study.

>> And I’m certainly very interested in Dill and Zilla’s best - it’s sort of like the NCI best case scenario, where he’s asking patients who believe that they’ve cured their cancer with cannabis alone, to complete a survey online, CATA, C-A-T-A survey.com, to present him with that information and allow him to review their medical record as well. So we can see if there’s any veracity or any potential for cannabis alone to have an impact on tumors. I think that’s an important study.

>> Also, at VCU we’re trying to get a pilot study underway to follow up on the nabiximols cancer pain study. I’m looking at a more homogeneous group of patients that have not been on opioids for a long time. But this has been work in progress, and present climate with the pandemic has slowed it down further.

>> So I think all of these trials sound phenomenal and I’m so excited for all the results. I’ll just throw in, as I referenced before at the Farber, we are doing a cannibidiol trial targeting scam-xiety which we know cancer patients suffer with and with the hope that one day maybe CBD will replace benzodiazepines which we know are terrible for the elderly.

>> Thank you every - oh, go ahead.

>> Sorry. There are some studies that are going on for the EVALI outbreak. So Dr. Braun mentioned that there are about 2,800 people. And in Utah, Dr. Callahan is doing a follow up study of the EVALI patients and doing patient reported outcomes and pulmonary function tests and other different exams.

>> Great, thank you everyone. This comes to the end of our session. Jeff, do you want to close it up?

>> Yes, thank you, Gary. Yeah, thank you so much to the panel for your work over the past four days. I think it’s been very enlightening and it gives us a lot to work on as we think about what has been, what’s transpired. So it’s been an excellent four days. My thanks to the co-chairs and speakers and the attendees for hanging in there for as much time as you were able to. It’s very - I would to point out it’s a very international meeting. We were able to pull together speakers from all over the U.S., from Europe, from Israel, and I’m sure attendees from many other places. And the information from the meeting will be very useful for - to us and the NCI, the program staff, to improve our ability to assess the scientific issues, and in grant applications, and thinking about potential value of any new initiatives. I want to remind people or inform people that we are planning a general supplement with articles to archive the presentations and the discussions that have gone on over the past four days which hopefully will stimulate more scientific dialogue. And the meeting’s also been recorded and will be made available on the events webpage and I think Jennifer will tell us more about that in a minute. So, just again, my thanks to everyone for all that you’ve done, and that I’d like then to turn it back over to Jennifer for final comments. Unless Jerry, you had any other comments you wanted to make?

>> I just want to echo you, and offer my thanks to everyone who participated in this conference, all of the session co-chairs as well as the speakers. And also folks who attended the conference and provided lively, robust dialogue for us to react to. So, thank you very much everyone.

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